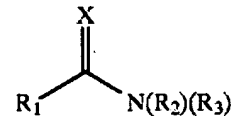
Amendments to the Claims:

This listing of claims will replace all prior versions, and listings of claims in the application.

Listing of Claims:

1. (Currently amended) A method of modulating an Edg-3 receptor mediated biological activity comprising contacting a cell expressing the Edg-3 receptor with an amount of ~~an~~ a modulator of the Edg-3 receptor sufficient to modulate the Edg-3 receptor mediated biological activity wherein the modulator is a compound of ~~the structural formula~~ Formula (I):

(I)



or a pharmaceutically ~~available~~ acceptable solvate or hydrate thereof, wherein;

each ~~of~~ R_1, R_2, and R_3 is independently selected from -H, -halo, $-NO_2$, -CN, $-C(R_5)_3$, $-(CH_2)_mOH$, $-N(R_5)(R_5)$, $-O(CH_2)_mR_5$, $-C(O)R_5$, $-C(O)NR_5R_5$, $-C(O)NH(CH_2)_m(R_5)$, $-OCF_3$, -benzyl, $-CO_2CH(R_5)(R_5)$, $-(C_1\text{-}C_{10})$alkyl, $-(C_2\text{-}C_{10})$alkenyl, $-(C_2\text{-}C_{10})$alkynyl, $-(C_3\text{-}C_{10})$cycloalkyl, $-(C_8\text{-}C_{14})$bicycloalkyl, $-(C_5\text{-}C_{10})$cycloalkenyl, $-(C_5)$heteroaryl, $-(C_6)$heteroaryl, $-(C_5\text{-}C_{10})$heteroaryl, -naphthyl, $-(C_3\text{-}C_{10})$heterocycle, $-CO_2(CH_2)_mR_5$, -N(OH)aryl, $-NHC(O)R_5$, $-NHC(O)OR_5$, $-NHC(O)NHR_5$, -heterocylcoalkyl, $-(C_1\text{-}C_{10})$alkylNHC(O)$(CH_2)_mR_5$, $-(C_1\text{-}C_{10})$alkylNR_5R_5, $-OC(O)(CH_2)_mCHR_5R_5$, $-CO_2(CH_2)_mCHR_5R_5$, $-OC(O)OR_5$, $-SR_5$, $-S(O)R_5$, $-S(O)_2R_5$, $-S(O)_2NHR_5$, ~~or~~ and

~~R_3 is -H $-C(R_5)_3$, $-(CH_2)_mOH$, $-C(O)R_5$, $-C(O)NR_5R_5$, $-C(O)NH(CH_2)_m(R_5)$, -benzyl, $-CO_2CH(R_5)(R_5)$, $-(C_1\text{-}C_{10})$alkyl, $-(C_2\text{-}C_{10})$alkenyl, $-(C_2\text{-}C_{10})$alkynyl, $-(C_3$-~~

~~C_{10})cycloalkyl, -(C_8-C_{14})bicycloalkyl, -(C_5-C_{10})cycloalkenyl, -(C_5)heteroaryl, -(C_6)heteroaryl, -(C_5-C_{10})heteroaryl, -naphthyl, -(C_3-C_{10})heterocycle, $-CO_2(CH_2)_mR_,$, -N(OH)aryl, -NHC(O)R_5, -NHC(O)OR_5, -NHC(O)NHR_5, -N=C(aryl), -heterocycloalkyl, -(C_1-C_{10})alkylNHC(O)$(CH_2)_mR_5$, -(C_1-C_{10})alkylNR_5R_5, $-OC(O)(CH_2)_mCHR_5R_5$, $-CO_2(CH_2)_mCHR_5R_5$, -OC(O)OR_5, -SR_5, -S(O)R_5, -$S(O)_2R_5$, -$S(O)_2NHR_5$, or and~~

wherein;

each R_5 and R_6 is independently selected from -halo, $-NO_2$, -CN, -OH, $-CO_2H$, -N(C_1-C_{10})alkyl(C_1-C_{10})alkyl, -O(C_1-C_{10})alkyl, -C(O)(C_1-C_{10})alkyl, $-C(O)NH(CH_2)_m$(C_1-C_{10})alkyl, $-OCF_3$, -benzyl, $-CO_2(CH_2)_mCH$((C_1-C_{10})alkyl(C_1-C_{10})alkyl), $-CO_2$(C_1-C_{10})alkyl, -(C_1-C_{10})alkyl, -(C_2-C_{10})alkenyl, -(C_2-C_{10})alkynyl, -(C_3-C_{10})cycloalkyl, -(C_8-C_{14})bicycloalkyl, -(C,-C_{10})cycloalkenyl, -(C_5)heteroaryl, -(C_6)heteroaryl, -phenyl, naphthyl, -(C_3-C_{10})heterocycle, $-CO_2(CH_2)_m$(C_1-C_{10})alkyl, $-CO_2(CH_2)_mH$, -NH-C(O)(C_1-C_{10})alkyl, -NHC(O)NH(C_1-C_{10})alkyl, -NH(aryl), -N=C(aryl), -OC(O)O(C_1-C_{10})alkyl, ~~or~~ and $-SO_2NH_2$;

X is selected from O, S, C(R_5)(R_5) ~~or~~ and N(R_5);

R_1, R_2 or R_3 taken in combination can form one or more substituted or unsubstituted 5 or 6 membered cyclic or heterocyclic rings or a 6-membered aromatic ring;

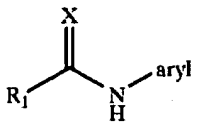
each m is independently an integer ranging from 0 to 8; and

each p is independently an integer ranging from 0 to 5.

2. (Currently amended) A method of modulating an Edg-3 receptor mediated biological activity in a subject comprising administering to the subject a therapeutically effective

amount of a modulator of the Edg-3 receptor wherein the modulator is a compound of ~~the structural formula~~ Formula ~~(~~(II):

(II)



or a pharmaceutically ~~available~~ acceptable solvate or hydrate thereof, wherein:

R_1 is selected from hydrogen, alkyl, substituted alkyl, acylamino, substituted acylamino, alkylamino, substituted alkylamino, alkylthio, substituted alkylthio, alkoxy, substituted alkoxy, alkylarylamino, substituted alkylarylamino, amino, arylalkyloxy, substituted arylalkyloxy, aryl, substituted aryl, arylamino, substituted arylamino, arylalkyl, substituted arylalkyl, dialkylamino, substituted alkyl amino, cycloalkyl, substituted cycloalkyl, cyclo-heteroalkyl, substituted cycloheteroalkyl, heteroaryloxy, substituted heteroaryloxy, heteroaryl, substituted heteroaryl, heteroalkyl, substituted heteroalkyl sulfonylamino ~~or~~ and substituted sulfonylamino;

X [[=]] is selected from O ~~or~~ and S.

3. (Original) The method of claim **1** or **2**, wherein the modulator is an agonist.

4. (Original) The method of claim **1** or **2**, wherein the modulator is an antagonist.

5. (Original) The method of claim **1** or **2**, wherein the modulator exhibits at least about 200 fold inhibitory selectivity for Edg-3 relative to other Edg receptors.

6. (Original) The method of claim **1** or **2**, wherein the modulator exhibits at least about 40 fold inhibitory selectivity for Edg-3 relative to other Edg receptors.

7. (Original) The method of claim **1** or **2**, wherein the modulator exhibits at least about 12 fold inhibitory selectivity for Edg-3 relative to other Edg receptors.

8. (Original) The method of claim **1** or **2**, wherein the modulator exhibits at least about 5 fold inhibitory selectivity for Edg-3 relative to other Edg receptors.

9. (Original) The method of claim **1** or **2**, wherein the modulator exhibits at least about 20 fold inhibitory selectivity for Edg-3 relative to other Edg receptors.

10. (Original) The method of claim **1** or **2**, wherein the modulator exhibits at least about 200 fold inhibitory selectivity for Edg-3 relative to Edg-4 and Edg-7 receptors.

11. (Original) The method of claim **1** or **2**, wherein the modulator exhibits at least about 40 fold inhibitory selectivity for Edg-3 relative to Edg-4 and Edg-7 receptors.

12. (Original) The method of claim **1** or **2**, wherein the modulator exhibits at least about 12 fold inhibitory selectivity for Edg-3 relative to Edg-4 and Edg-7 receptors.

13. (Original) The method of claim **1** or **2**, wherein the modulator exhibits at least about 5 fold inhibitory selectivity for Edg-3 relative to Edg-4 and Edg-7 receptors.

14. (Original) The method of claim **1** or **2**, wherein the biological activity is cell proliferation.

15. (Original) The method of claim **14**, wherein the modulator exhibits at least about 200 fold inhibitory selectivity for Edg-3 relative to other Edg receptors.

16. (Original) The method of claim **14**, wherein the modulator exhibits at least about 5 fold inhibitory selectivity for Edg-3 relative to other Edg receptors.

17. (Original) The method of claim **14**, wherein the modulator exhibits at least about 200 fold inhibitory selectivity for Edg-3 relative to Edg-4 and Edg-7 receptors.

18. (Original) The method of claim **14**, wherein the modulator exhibits at least about 5 fold inhibitory selectivity for Edg-3 relative to Edg-4 and Edg-7 receptors.

19. (Original) The method of claim **14**, wherein cell proliferation leads to ovarian cancer, peritoneal cancer, endometrial cancer, cervical cancer, breast cancer, colon cancer or prostrate cancer.

20. (Original) The method of claim **14**, wherein cell proliferation is stimulated by SPl.

21. (Original) The method of claim **1** or **2**, wherein the biological activity is calcium mobilization, VEGF synthesis, IL-8 synthesis, platelet activation, cell migration, phosphoinositide hydrolysis, inhibition of cAMP formation, actin polymerization, apoptosis, angiogenesis, inhibition of wound healing, inflammation, cancer invasiveness, suppressing autoimmune responses, or atherogenesis.

22. (Original) The method of claim **1** or **2** wherein the modulator binds to the Edg-3 receptor with a binding constant of at least about 10 nm.

23. (Original) The method of claim **1** or **2** wherein the modulator binds to the Edg-3 receptor with a binding constant between about 1 μM and 100 fM.

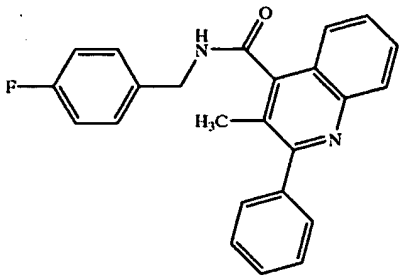
24. (Original) The method of claim **1** or **2**, wherein the modulator is a nucleic acid, protein or carbohydrate.

25. (Original) The method of claim **1** or **2**, wherein the modulator is an organic molecule of molecular weight of less than 750 daltons.

26. (Original) The method of claim **1**, wherein the cell is a hepatoma cell, an ovarian cell, an epithelial cell, a fibroblast cell, a neuronal cell, a carcinoma cell, a pheochromocytoma cell, a myoblast cell, a platelet cell or a fibrosarcoma cell.

27. (Original) The method of claim **21**, wherein the cell is OV202 human ovarian cell, a HTC rat hepatoma cell, a CAOV-3 human ovarian cancer cell, MDA-MB-453 breast cancer cell, MDA-MB-231 breast cancer cell, HUVEC cells A431 human epitheloid carcinoma cell or a HT 1080 human fibrosarcoma cell.

28. (Currently amended) The method of claim **25** wherein the modulator has a ~~the following structural~~ formula selected from:



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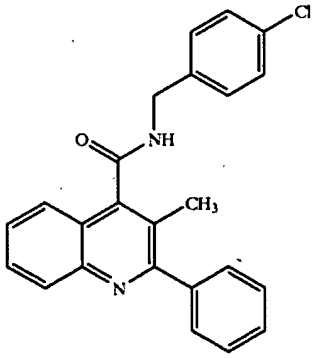

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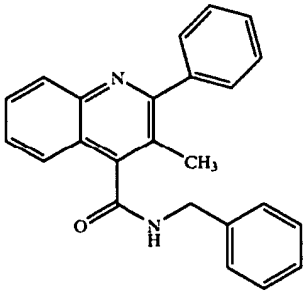

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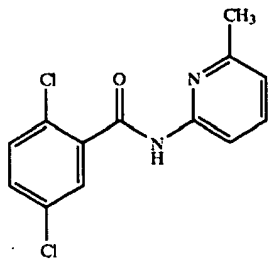

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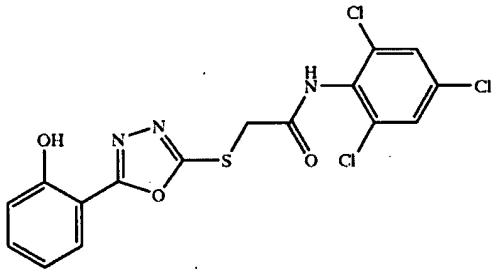
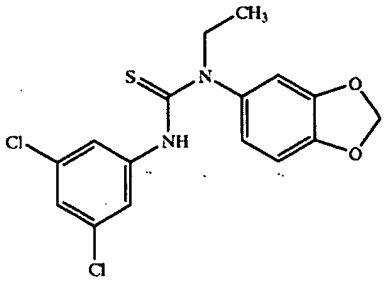


7 111 ; and



8 121 .

1 **29.** (Currently amended) A method for treating or preventing cancers, acute lung
2 diseases, acute inflammatory exacerbation of chronic lung diseases, surface epithelial cell injury,
3 or cardiovascular diseases in a patient in need of said treatment or said prevention, said method
4 comprising administering to ~~a~~ said patient ~~in need of such treatment or prevention~~ a
5 therapeutically effective amount of a compound of ~~structural formula~~ Formulae (I) or (II).

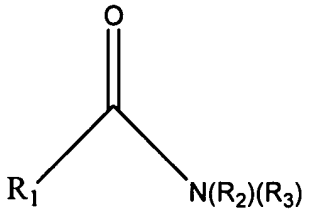
1 **30.** (Currently amended) A method for treating or preventing ovarian cancer,
2 peritoneal cancer, endometrial cancer, cervical cancer, breast cancer, colorectal cancer, uterine

cancer, stomach cancer, small intestine cancer, thyroid cancer, lung cancer, kidney cancer, pancreas cancer, ~~prostrate~~ prostate cancer, adult respiratory distress syndrome (ARDS), asthma, transcorneal freezing, cutaneous burns, ischemia or ~~artheselerosis~~ atherosclerosis in a patient in need of said treatment or said prevention, said method comprising administering to ~~a~~ said patient ~~in need of such treatment or prevention~~ a therapeutically effective amount of a compound of ~~structural formula~~ Formulae (I) or (II).

31. (Currently amended) A method for treating or preventing cancers, acute lung diseases, acute inflammatory exacerbation of chronic lung diseases, surface epithelial cell injury, or cardiovascular diseases in a patient in need of said treatment or said prevention, said method comprising administering to ~~a~~ said patient ~~in need of such treatment or prevention~~ a therapeutically effective amount of a compound of ~~structural formula~~ Formulae (I) or (II) and one or more agonists or antagonists of an Edg-3 receptor.

32. (Currently amended) A method for treating or preventing cancers, acute lung diseases, acute inflammatory exacerbation of chronic lung diseases, surface epithelial cell injury, or cardiovascular diseases in a patient in need of said treatment or said prevention, said method comprising administering to ~~a~~ said patient ~~in need of such treatment or prevention~~ a therapeutically effective amount of a compound of ~~structural formula~~ Formulae (I) or (II) and one or more drugs useful in treating or preventing cancers, acute lung diseases, acute inflammatory exacerbation of chronic lung diseases, surface epithelial cell injury, or cardiovascular diseases.

33. (New) A method of treating cardiovascular disease in a patient comprising:
administering to the patient a therapeutically effective amount of a modulator of an Edg-3 receptor wherein the modulator is a compound of Formula (III):

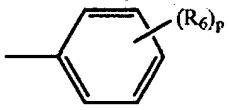


(III)

or a pharmaceutically acceptable solvate or hydrate thereof, wherein

R_1 is a $(C_5\text{-}C_{10})$heteroaryl group;

each R_2 and R_3 is independently selected from -H, -halo, $-NO_2$, -CN, $-C(R_5)_3$, $-(CH_2)_mOH$, $-N(R_5)(R_5)$, $-O(CH_2)_mR_5$, $-C(O)R_5$, $-C(O)NR_5R_5$, $-C(O)NH(CH_2)_m(R_5)$, $-OCF_3$, -benzyl, $-CO_2CH(R_5)(R_5)$, $-(C_1\text{-}C_{10})$alkyl, $-(C_2\text{-}C_{10})$alkenyl, $-(C_2\text{-}C_{10})$alkynyl, $-(C_3\text{-}C_{10})$cycloalkyl, $-(C_8\text{-}C_{14})$bicycloalkyl, $-(C_5\text{-}C_{10})$cycloalkenyl, $-(C_5)$heteroaryl, $-(C_6)$heteroaryl, $-(C_5\text{-}C_{10})$heteroaryl, -naphthyl, $-(C_3\text{-}C_{10})$heterocycle, $-CO_2(CH_2)_mR_5$, -N(OH)aryl, $-NHC(O)R_5$, $-NHC(O)OR_5$, $-NHC(O)NHR_5$, -heterocylcoalkyl, $-(C_1\text{-}C_{10})$alkylNHC(O)$(CH_2)_mR_5$, $-(C_1\text{-}C_{10})$alkylNR_5R_5, $-OC(O)(CH_2)_mCHR_5R_5$, $-CO_2(CH_2)_mCHR_5R_5$, $-OC(O)OR_5$, $-SR_5$, $-S(O)R_5$, $-S(O)_2R_5$, $-S(O)_2NHR_5$, and



wherein

each R_5 and R_6 is independently selected from -halo, $-NO_2$, -CN, -OH, $-CO_2H$, $-N(C_1\text{-}C_{10})$alkyl$(C_1\text{-}C_{10})$alkyl, $-O(C_1\text{-}C_{10})$alkyl, $-C(O)(C_1\text{-}C_{10})$alkyl, $-C(O)NH(CH_2)_m(C_1\text{-}C_{10})$alkyl, $-OCF_3$, -benzyl, $-CO_2(CH_2)_mCH((C_1\text{-}C_{10})$alkyl$(C_1\text{-}C_{10})$alkyl), $-CO_2(C_1\text{-}C_{10})$alkyl, $-(C_1\text{-}C_{10})$alkyl, $-(C_2\text{-}C_{10})$alkenyl, $-(C_2\text{-}C_{10})$alkynyl, $-(C_3\text{-}C_{10})$cycloalkyl, $-(C_8\text{-}C_{14})$bicycloalkyl, $-(C,\text{-}C_{10})$cycloalkenyl, $-(C,)$heteroaryl, $-(C_6)$heteroaryl, -phenyl, naphthyl, $-(C_3\text{-}C_{10})$heterocycle, $-CO_2(CH_2)_m(C_1\text{-}C_{10})$alkyl, $-CO_2(CH_2)_mH$, -NH-

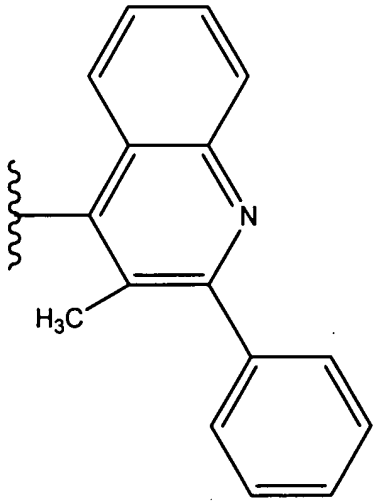
$C(O)(C_1\text{-}C_{10})$alkyl, -NHC(O)NH$(C_1\text{-}C_{10})$alkyl, -NH(aryl), -N=C(aryl), -OC(O)O$(C_1\text{-}C_{10})$alkyl, and $-SO_2NH_2$;

R_2 or R_3 taken in combination can form one or more substituted or unsubstituted 5 or 6 membered cyclic or heterocyclic rings or a 6-membered aromatic ring;

each m is independently an integer ranging from 0 to 8; and

each p is independently an integer ranging from 0 to 5.

34. (New) The method of claim **33**, wherein R_1 is

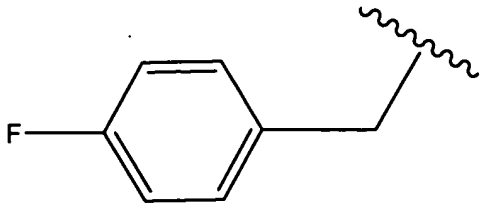


35. (New) The method of claim **34**, wherein R_2 is H.

36. (New) The method of claim **35**, wherein R_3 is a benzyl group.

37. (New) The method of claim **36**, wherein said benzyl group is a substituted benzyl group.

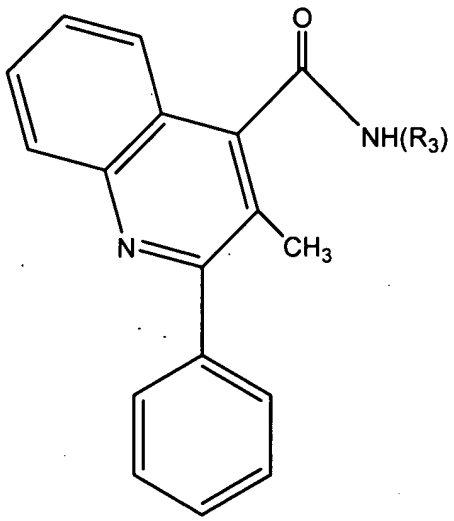
38. (New) The method of claim **37**, wherein said substituted benzyl group is



39. (New) The method of claim **33**, wherein said cardiovascular disease is selected from the group consisting of ischemia and atherosclerosis.

40. (New) A method of treating cardiovascular disease in a patient comprising:

administering to the patient a therapeutically effective amount of a modulator of an Edg-3 receptor wherein the modulator is a compound of Formula (IV):

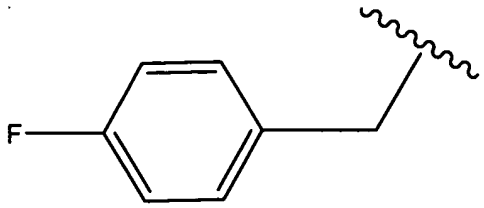


(IV)

or a pharmaceutically acceptable solvate or hydrate thereof, wherein

R_3 is a substituted benzyl group.

41. (New) The method of claim **40**, wherein said substituted benzyl group is



42. (New) The method of claim **40**, wherein said cardiovascular disease is selected from the group consisting of ischemia and atherosclerosis.